IN THE SPECIFICATION

Please replace page 3, paragraph 3 with:

The LDL-r synthesis is regulated by a sophisticated feedback mechanism that controls the transcription of the LDL-r gene in response to variations in the intracellular sterol concentration and the cellular demand for cholesterol (Sudhof TC et al J Biol Chem 1987; 262:10773-10779). DNA motifs necessary for transcriptional regulation of the LDL-r gene are located within 177 bp of the proximal promoter (Sudhof TC et al. J Biol Chem 1987; 262: 10773-10779). This region contains all the cis-acting elements for basal expression and sterol regulation and includes three imperfect direct repeats of 16 bp each. Repeat 1 and 3 containing binding sites for the transcriptional factor Sp1 and are essential for producing the basal expression of the gene but require the contribution of the repeat 2 for full expression (Dawson PA et al. J Biol Chem 1988; 263;3372-3379). Repeat 2 contains a 10 bp regulatory element , SRE-1, (Smith JR et al. J Biol Chem 1990; 265:2306-2310) that allows binding of the transcriptional factor designated as SREBP-1, when the intra-cellular sterol concentration diminishes. To date, several naturally-occurring mutations have been mapped to the transcriptional regulatory elements of the LDL gene receptor (Hobbs HH, et al. Hum Mutat 1992; 1:445-466; Koivisto UM, et al ProcNatl Acad Sci USA, 1994; 91:10526-10530), Mozas P, et al J Lipid Res 2002; 43:13-18, ~~http://www.ucl.ac.uk/fh; http://www.umd.necker.fr)~~ (worldwideweb: ucl.ac.uk/fh; worldwideweb:umd.necker.fr.)

Please replace page 4, paragraph 1 with:

Exon 1 encodes the signal peptide, a sequence of 21 amino acids, which is cleaved from the protein during the translocation into the endoplasmic reticulum. Several frameshift, missense and nonsense mutation has been described in this exon ~~http://www.ucl.ac.uk/fh; http://www.umd.necker.fr)~~ (worldwideweb: ucl.ac.uk/fh; worldwideweb: umd.necker.fr.)

Please replace page 4, paragraph 3 with:

The second domain of the human LDL-r consists of 400 amino acid sequence, encoded by exons 7 to 14. This sequence shows a 33% of homology of the epidermal growth factor precursor (EGFP). Like the ligand binding domain, this region also contains three repeats of 40 amino acids with cysteine-rich sequences. The first two repeats, designated A and B, are contiguous and separated from the third repeat, by a 280 amino acid region that contains five copies of the YWTD (Tyr-Trp-Thr-Asp) sequence. The EGFP like domain is fundamental for the acid–dependent dissociation of the LDL particles from the LDL-r and clathrin coat pits that takes place in the endosome during receptor recycling. Of the all mutations described to date, approximately 55% are located in the EGFP-homology region and 35% among the YWTD repeats ~~(http.//www.ucl.ac.uk/fh)~~ worldwideweb:ucl.ac.uk/fh; worldwideweb:umd.necker.fr.)

Page 35, line 16 as numbered, please replace with:

~~**R279G mutation analisis**~~ **R279G mutation analysis**

Page 46, line 21 as numbered, please replace with:

~~**Análisis of the mutation T446I**~~ **Analysis of the mutation T446I**

Page 47, line 14 as numbered, please replace with:

~~**Análisis de la mutación 1423delGC/insA**~~ **Analysis Mutant 1423delGC/insA**

Page 49, line 4 as numbered, please replace with:

~~**Análisis of the mutation**~~ **[1587-5del5; ~~1587del31]~~ Analysis of the mutation [1587-5del5; 1587del31]**

Delete the Sequence Listing presently of record and replace, on a separate page after page 65, last line with the Sequence Listing attached hereto.